Remarks

Claims

Entry and consideration of claims 15-17 is respectfully requested.

Claim rejections under 35 U.S.C. §103

Claims 15-17 were rejected under 35 U.S.C. §103(a) as being unpatentable over King et al. (US2004/0014202) in view of Pinkel et al. (US 5,837,196) and Glazer et al. (US 6,150,107).

Before commenting on the prior art, Applicants would like to explain once more the principle of operation of the invention. The invention aims at a real time PCR instrument for detecting maximum fluorescence emission of at least five different fluorescent compounds. Referring to Figure 4 as an example of possible embodiment for the instrument of the invention, the instrument has an excitation unit comprising a light source (LED) that emits light toward a reaction vessel. A lightpipe is arranged for receiving the light from the reaction vessel and is capable of distributing this light homogeneously to a fiber bundle. The fiber bundle (at least 5) transmits this light to at least 5 separate fluorescent detector entities in the detection unit, each of said detector entities having central detection wavelengths distinct from each other by at least 25 nm. The instrument has also means for heating and cooling and multiple reaction vessels to conduct the necessary heating and cooling steps of the PCR reaction. The excitation and the detection units are located in separate housings.

There are many advantages provided by the specific arrangement of the instrument according to the invention. One of these advantages is that only one light source, e.g. a monochromatic light source such as for example a LED emitting at 470 nm, is potentially necessary for detecting the fluorescence of at least 5 different fluorescent compounds simultaneously in multicolor real time PCR reactions. The instrument requires neither multiple excitation light sources (with different wavelengths) nor filters for exciting different fluorescent compounds. Because the excitation and detection units are decoupled and separated by using optical fibers and because a lightpipe homogeneously distributes the light to these fibers, highly precise positioning of the excitation unit towards the reaction vessel can be achieved without moving the detection unit. Also, the number of necessary dichroic mirrors is minimized by this arrangement.

This is clearly stated on page 17, lines 19-27 of the patent application as filed:

"This set up of excitation unit and detection unit located in separate housings provides two advantages compared to the optical unit as disclosed in WO 97/46712: Homogeneous distribution of emitted light into all six detection channels and mechanical decoupling of the excitation and detection unit. This enables highly precise positioning of the excitation unit towards the reaction vessels to become monitored (e. g. capillary tips) without moving the detection unit. Moreover, the number of necessary dichroic mirrors is minimized. An example of such a set up is shown in fig. 4, which discloses a possible embodiment of the invention. As it can be seen, excitation and detection unit are located in different housings."

Applicants believe that these features are fully reflected in amended claim 15 and that the Office Action fails to completely appreciate all the features of claim 15.

In particular, the Office Action alleges that King et al. discloses a real time PCR instrument. Applicants respectfully disagree. Claim 1 covers a real time PCR instrument, not a device for real time PCR. King et al. teach a device that can be used in a PCR instrument, but not a PCR instrument *per se*.

The Office Action alleges that King et al. teach a device having a detection unit comprising at least 5 separate fluorescent detector entities, each of said detector entities having a central detection wavelength distinct from each other by at least 25 nm. However, King et al. does not teach specifically that the central detection wavelength of these detector entities must be distinct from each other by at least 25 nm. King et al. only discloses different dyes, having different emission wavelengths and detectors, some of them could be separatedy by more than 25 nm in their wavelengths. Further, in paragraph [0078], King et al. describes that when multiple OLED are used, they are capable of producing excitation wavelengths at four different frequencies, implying the identification of only four distinct fluorescent compounds, not five.

The Office Action alleges that King et al. teaches a lightpipe being arranged for receiving light from the reaction vessel and capable of distributing homogeneously said light for transmission to optical fiber bundles. The Office Action relies on paragraph [0043] of King et

al. Applicants respectfully disagree. A careful reading of paragraph [0043] of King et al. teaches that the device for carrying wavelengths is either a lightpipe or fiber optics, mirror, and/or lenses, not a combination of a lightpipe and optical fibers. Further, King et al. fails to disclose 5 optical fiber bundles. Also, and in any cases, King et al. fails to teach the specific location of the optical fibers toward the lightpipe and their interaction with the lightpipe, i.e. King et al. fails to teach that the lightpipe receives light from the reaction vessel and that the light is then distributed to the optical fiber bundles (and not the other way around for example).

The Office Action also alleges that in Fig. 7, King et al. teaches a device wherein the excitation and detection units are located in separate housings. Applicants respectfully disagree. The excitation unit of the device of the invention comprises at least one light source and a lightpipe and the detection unit comprises detector entities. Thus, in the device of the invention, the excitation unit (light source + a light pipe) are located in a housing on the one hand and the detectors are located in a separate housing on the other hand. Fig. 7 in King et al. does not teach this specific arrangement. Fig. 7 in King et al. teaches a light source, two lightpipes and two detectors. In Fig. 7, the excitation unit (light source + lightpipe) are not located in a housing that is separate from the detectors. Further, the detectors are not located in a housing.

In fact, King et al. fails to teach some of the most critical elements of the instrument of the invention. As explained above, the fact that the excitation and detection units are located in separate housings and linked by optical fibers provide benefits that King et al. failed to appreciate.

Pinkel et al. teach a bundle of optical fibers dipped in the reaction medium and transmitting directly the light emitted from the reaction vessel to multiple detectors. Apart from teaching the use of optical fibers in a detection method, Pinkel et al. does not provide any teaching that could be useful to arrive at the invention. In particular, the device taught in Pinkel et al. is completely inadequate for the intended purpose of the instrument according to the invention, which is detecting the fluorescence of at least 5 different fluorescent compounds simultaneously in multicolor real time PCR reactions. There is no element allowing a real time PCR reaction in the device taught by Pinkel et al. Further, Pinkel et al. does not teach the benefits of the instrument according to the invention regarding the separation of the excitation and detection units in separate housings either, the precision obtained and the minimization of

dichroic mirrors. Therefore, the person skilled in the art would not even have been motivated to take into account the teaching of Pinkel et al. to arrive at the invention.

Glazer et al. does not provide any additional teaching in this regard either.

Even by combining King et al. with Pinkel and Glazer, some of the most critical elements of the instrument of the invention as recited above are still missing. In particular, all of King et al. with Pinkel and Glazer fail to teach an excitation unit and a detection unit that are located in separate housings and the benefits associated thereto as explained above. Even by combining the teaching of all three references, the person skilled in the art would still miss this critical teaching and would therefore also miss the motivation to implement this critical feature in a PCR instrument.

Applicants therefore respectfully submit that the instrument as presently claimed in claim 15 is not obvious over the prior art of records. Reconsideration and withdrawal of the obviousness rejection of claim 15 under §103(a) as being unpatentable over King et al. (US2004/0014202) in view of Pinkel et al. (US 5,837,196) and Glazer et al. (US 6,150,107) is respectfully requested.

Claims 16 and 17 depend upon claim 15 and therefore incorporate each and every limitation of that claim. For the reasons set forth with respect to claim 15, withdrawal of the rejections of the dependent claims 16 and 17 is also respectfully requested.

Conclusion

The present Amendment is accompanied with a Request for Continued Examination. The Commissioner is authorized to charge the RCE fee under 37 CFR § 1.17(e) required for this submission to Deposit Account No. 500812. Therefore Applicants respectfully request the finality of the Final Office Action mailed April 15, 2009 to be withdrawn.

Applicants believe that the present application is now in condition for allowance. No other fee is believed to be due at this time. The Commissioner is further authorized to charge any fee deficiency or credit any overpayment to the Deposit Account No. 500812.

If the Examiner believes that a telephone call would expedite prosecution of this application, the Examiner is invited to call the undersigned directly at the number below.

Respectfully submitted,

/Vivien M. Banholzer/

Date: June 11, 2009

Vivien M. Banholzer (Reg. No. L0508)

Roche Molecular Systems, Inc.
4300 Hacienda Drive
Pleasanton, CA 94588
Tel. 925-730-8565
Fax 925-225-1128